

Central Risk Estimates at Low Doses: Issues and Approaches

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A central estimate of the risk at low doses is an important part of a quantitative characterization of risk for human health assessments. Central or expected value estimates of risk play a critical role in cost-benefit analysis. However, the maximum likelihood estimate (MLE) of the risk at low doses can be very unstable when a dose-response model with a linear term is used. Change of just one animal death in one of the groups could cause the estimated risk to change several orders of magnitude.

A greater stability of the estimated risks at low doses could be achieved by using data from many bioassays. Unfortunately, multiple bioassay data are rarely available. The National Center for Environmental Assessment (NCEA) is investigating several approaches to address instability of the risk at low-dose estimates using statistical methods that are applicable to the results of a single bioassay experiment. This presentation discusses a parametric resampling procedure based on bootstrap that is shown to address instability of the MLE of the risk at low doses. Methods informed by Bayesian analysis using Markov Chain Monte Carlo (MCMC) are also discussed. These statistical approaches allow us to make inferences about distribution of the risk at low doses.

The developed procedures are applied to simulated data as well as actual data from Integrated Risk Information System (IRIS) assessments. The distribution of the risk estimator at low doses is described. Stable central (expected value) estimates of the risk at low doses that are robust against a small change in the observed bioassay data are suggested. Their merits and further characterization are discussed.

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